

**REMARKS**

Claims 63-66 and 69 are objected to for the reasons set forth in the Official Action. In accordance with the Examiner's suggested claim amendments and proposed language, these claims are now rewritten as new claims 88 -91 and 94.

Next, claims 61-73 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for the reasons noted in the official action. The rejected claims are accordingly amended, by the newly rewritten claims, and the presently pending claims are now believed to particularly point out and distinctly claim the subject matter regarded as the invention, thereby overcoming all of the raised § 112, second paragraph, rejections. The Applicant thanks the Examiner for the proposed independent claim language and suggestions to overcome the 35 U.S.C. § 112, second paragraph, issues raised by the Examiner. Accordingly, the Applicant has canceled the pending claims and rewritten the claims 61-86 as new claims 87-112 (where claims 100-112 are currently withdrawn), and new independent claims 87 and 96 correspond to previous independent claims 61 and 70 respectively and now substantially incorporate the Examiner's suggested claim language.

Claims 61-64, 66, 68 and 70-72 are rejected, under 35 U.S.C. § 103(a), as being unpatentable over Bader WO-01/09282, hereinafter Bader '282. The Applicant acknowledges and respectfully traverses the raised obviousness rejection in view of the following remarks.

As an initial matter, the Applicant wishes to address the fact that the problem to be solved by Bader '282 is significantly different than the problem solved by any known bioreactor. Bader '282 is concerned with simplifying and improving known cell culturing chambers comprising a carrier and a variable chamber volume obtainable by an elastic membrane or film whereby the medium and cells are located in the space *between* the carrier and the membrane or film. Bader '282 provides a cell culture device with a flat cell culture chamber with a minimum film density (even in a curved tube form as shown in Bader '282 Figs. 7 and 8),

whereby the film guarantees the elasticity of the culture chamber. The problem to be solved, and the solution disclosed by the present invention are both substantially different from Bader '282 and thus a person of ordinary skill in the art would not look to Bader '282 to achieve the presently claimed invention as explained below.

The presently claimed invention relates to a bioreactor which can be formed into a variety of complex shapes and specific sizes by forming a support material layer and an external boundary layer impermeable to living cells. The support structure and boundary layer precisely define the shape and the size of the cell culture chamber. As discussed at paragraph [011] of the current application the interior of the Applicant's porous support structure **is the cell culture chamber or bioreactor itself**. In the known bioreactor's, just as Bader '282, these references clearly teach that the reactor culture chamber 11a and the support or carrier device are different and separate structures. As recited in Applicant's claim 87, the living cells are introduced, "...into the porous support structure *which constitutes the cell culture chamber*;" This improvement where the cell support structure and the cell culture chamber are one and the same, is particularly advantageous with implant and prosthesis applications where a complex shape and/or specific size is needed because the cell culture shape and size are precisely defined by the aforementioned external boundary layer.

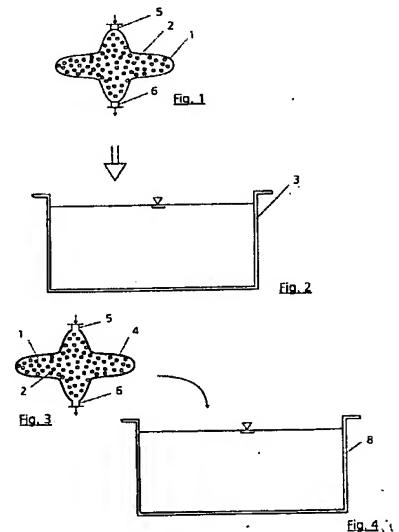
As the Examiner is aware, in order to properly support an obviousness rejection under 35 U.S.C. §103(a) the cited prior art reference must provide some disclosure, teaching or suggestion which would lead one of skill in the art to achieve each and every recited step and feature of the presently claimed invention. We reiterate as in previous response that Bader '282 has a flexible exterior wall and is fundamentally different than the presently claimed boundary layer. Elastic exterior walls allow the cell culture to grow and do not define a precise shape, which is one of the main points of our invention. Be that as it may, the Applicant's invention is

particularly different from Bader '282 both structurally and functionally as explained in further detail below along with the noted claim features.

Importantly, the Applicant notes that while Bader '282 arguably teaches the injecting, or placing of an extra-cellular matrix such as calcareous structures within the cell chamber space 11a as described at page 11, first full paragraph, the method by which this is done in accordance with the disclosed structure of Bader '282 defining the cell chamber space 11a between a carrier plate 1 and a flexible film 2, is entirely different from the method and structure of the presently claimed invention.

In the present invention the porous support material is formed into a desired shape and size to form a desired human body part. The boundary layer is applied directly to the exterior of the porous support material and encompasses or encloses the support material entirely within a contiguous outer boundary layer. This aspect of the present invention, as clearly seen in the Applicant's Figures reproduced below, encompasses the entire underlying support material (as it must to form the requisitely shaped and sized human body part) and is a seamless, contiguous boundary, interrupted only by the nutrient inlet and outlet flow channels.

Whether or not Bader '282 discloses such a step of forming a porous support structure and placing the extracellular matrix within the chamber space 11a, Bader '282 certainly does not disclose a contiguous outer boundary layer "encapsulating the entire porous support material by means of a boundary layer of cell-impermeable material:" as specifically recited in claim 87. In other words, the applied reference teaches an entirely different method and structure for obtaining a tissue structure than the dipping process and resulting structure as in the presently claimed invention.

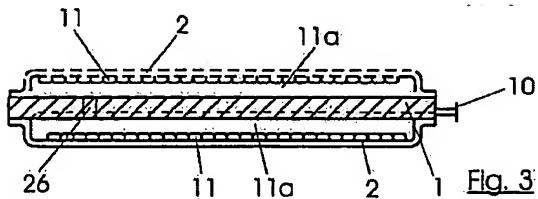


In all of the embodiments disclosed by Bader '282, the cell culture chamber 11a is formed *between* a carrier plate 1 and a flexible film 2 wherein the chamber 11a is defined by an edge connection, or clamping, of the flexible film 2 to outer edge of the carrier plate 1 (or carrier frame 1a). As discussed at page 5, first full paragraph, "In a basic design, the device has a moldable carrier plate, which is principally composed of plastic, as carrier 1. A gas-permeable and flexible plastic film 2 is applied to the carrier plate 1 and is tightly connected to the edges of the carrier plate 1". Also, at page 6, first full paragraph, "The flexible film 2 can be connected to the carrier plate 1 at the edges in any suitable manner, for example by clamping, bonding, welding or bolting".

The Applicant can find no deviation from this basic structure in any of the other embodiments disclosed by Bader '282. Even in the embodiment shown in FIGS. 7 and 8 where this basic structure is maintained where" . . . the frame construction shown in FIG. 4 can be curved to form a circle as depicted in principle in FIG. 7, or else in the spiral shape as can be seen in FIG. 8 " . . . result in a flexible system in the form of a tube with an [sic] in each case one carrier plate or one carrier ring 1b and films 2 and 3 in between, in whose interior the cell culture 11a is present". Page 12, first full paragraph, lines 11-20.

In order to clarify the present invention from the cited reference, and in accordance with the above remarks, the Applicant has added the step of "b) encapsulating the entire porous support structure by means of a boundary layer of cell-impermeable material" to the newly rewritten independent claims. Such a feature is not disclosed, taught or suggested in any manner by Bader '282. Bader '282 explicitly teaches the fastening of the films 2 and 3 to the edges of the carrier plate 1 or carrier frame 1a on one side of the carrier plate and therefore, even where the carrier plate 1 is formed as a tube, the film(s) cannot entirely enclose, or encapsulate, the carrier frame 1 as now recited in claims 87 and 96. Secondly, even in the embodiment of FIG. 3 in Bader '282, the carrier plate 1 is not entirely encapsulated, nor is the

outer boundary layer (elastic film 2) contiguous as there is a separate piece of film 2 individually fastened to each side of the carrier plate 1.



Support for the step of "encapsulating the entire porous support structure..." can be found throughout the Applicant's specification. The process as disclosed in the Applicant's FIGS. 1-4 shown above, as well as the related description at least a paragraphs [031] -[036] dictate the encapsulating and contiguous nature of the outer boundary layer and thus, such recitation is not believed to be new matter.

If any further amendment to this application is believed necessary to advance prosecution and place this case in allowable form, the Examiner is courteously solicited to contact the undersigned representative of the Applicant to discuss the same.

In view of the above amendments and remarks, it is respectfully submitted that all of the raised obviousness and indefinite rejections should be withdrawn at this time. If the Examiner disagrees with the Applicant's view concerning the withdrawal of the outstanding rejections or applicability of the Bader '282 reference, the Applicant respectfully requests the Examiner to indicate the specific passage or passages, or the drawing or drawings, which contain the necessary teaching, suggestion and/or disclosure required by case law. As such teaching, suggestion and/or disclosure is not present in the applied references, the raised rejection should be withdrawn at this time. Alternatively, if the Examiner is relying on his/her expertise in this field, the Applicant respectfully requests the Examiner to enter an affidavit substantiating the Examiner's position so that suitable contradictory evidence can be entered in this case by the Applicant.

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In view of the foregoing, it is respectfully submitted that the raised rejection(s) should be withdrawn and this application is now placed in a condition for allowance. Action to that end, in the form of an early Notice of Allowance, is courteously solicited by the Applicant at this time.

The Applicant respectfully requests that any outstanding objection(s) or requirement(s), as to the form of this application, be held in abeyance until allowable subject matter is indicated for this case.

In the event that there are any fee deficiencies or additional fees are payable, please charge the same or credit any overpayment to our Deposit Account (Account No. 04-0213).

Respectfully submitted,



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